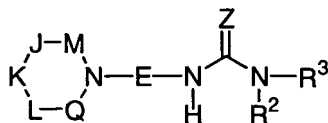


What is Claimed is:

1. A compound of formula (I):



5

(I)

or stereoisomers or pharmaceutically acceptable salts thereof, wherein:

10 M is absent or selected from CH_2 , CHR^5 , CHR^{13} , $\text{CR}^{13}\text{R}^{13}$, and CR^5R^{13} ;

Q is selected from CH_2 , CHR^5 , CHR^{13} , $\text{CR}^{13}\text{R}^{13}$, and CR^5R^{13} ;

15 K is selected from CH_2 , CHR^5 and CHR^6 ;

J and L are independently selected from CH_2 , CHR^5 , CHR^6 , CR^6R^6 and CR^5R^6 ;

20 with the provisos:

1) at least one of M, J, K, L, or Q contains an R^5 ;
and

25 2) when M is absent, J is selected from CH_2 , CHR^5 , CHR^{13} , and CR^5R^{13} ;

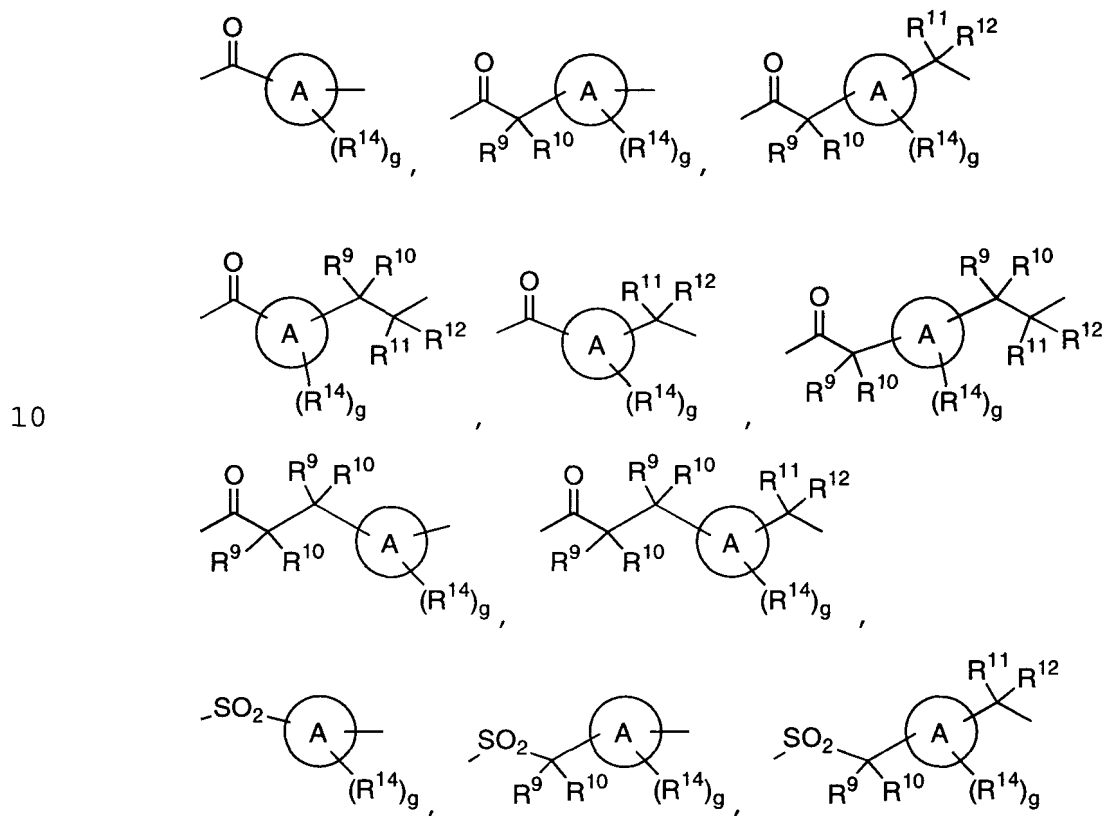
Z is selected from O, S, NR^{1a} , $\text{C}(\text{CN})_2$, $\text{CH}(\text{NO}_2)$, and CHCN ;

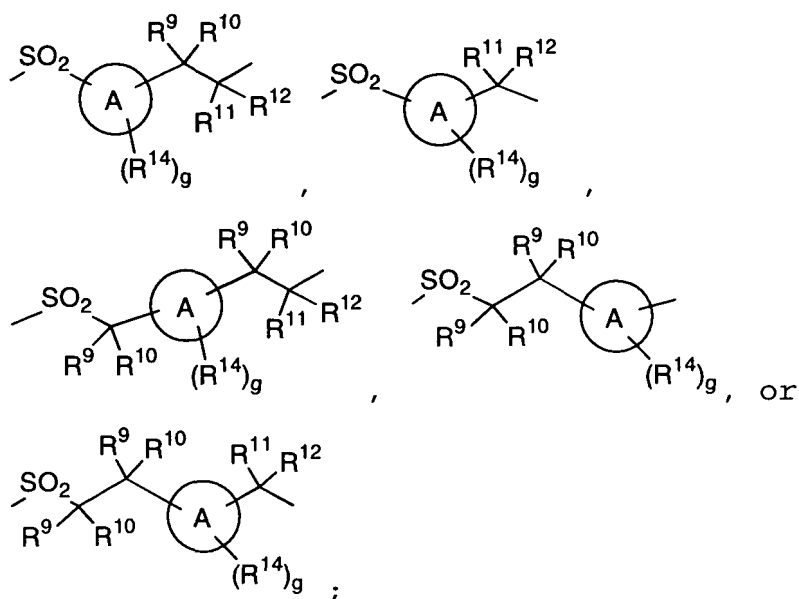
30

R^{1a} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $\text{CONR}^{1b}\text{R}^{1b}$, OR^{1b} , CN, NO_2 , and $(\text{CH}_2)_w\text{phenyl}$;

R^{1b} is independently selected from H, C_{1-3} alkyl, C_{3-6} cycloalkyl, and phenyl;

5 E is $-(C=O)-(CR^9R^{10})_v-(CR^{11}R^{12})-$, $-(SO_2)-(CR^9R^{10})_v-$
 $(CR^{11}R^{12})-$,





5

Ring A is a C₃₋₈ carbocyclic residue;

R² is selected from H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, and a (CH₂)_r-C₃₋₁₀ carbocyclic residue substituted with 0-5 R^a;

10

R^a, at each occurrence, is selected from C₁₋₄ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, Br, I, F, (CF₂)_rCF₃, NO₂, CN, (CH₂)_rNR^bR^b, (CH₂)_rOH, (CH₂)_rOR^c, (CH₂)_rSH, (CH₂)_rSR^c, (CH₂)_rC(O)R^b, (CH₂)_rC(O)NR^bR^b, (CH₂)_rNR^bC(O)R^b, (CH₂)_rC(O)OR^b, (CH₂)_rOC(O)R^c, (CH₂)_rCH(=NR^b)NR^bR^b, (CH₂)_rNHC(=NR^b)NR^bR^b, (CH₂)_rS(O)_pR^c, (CH₂)_rS(O)₂NR^bR^b, (CH₂)_rNR^bS(O)₂R^c, and (CH₂)_rphenyl;

15

20

R^b, at each occurrence, is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl;

R^C , at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^3 is selected from $(CH_2)_rN(CH_3)_2$, a $(CR^{3'}R^{3''})_r-C_{3-8}$ carbocyclic residue substituted with 0-5 R^{15} ; a $(CR^{3'}R^{3''})_r-C_{9-10}$ carbocyclic residue substituted with 0-4 R^{15} ; and a $(CR^{3'}R^{3''})_r-5-10$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15} ;

$R^{3'}$ and $R^{3''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^5 is selected from a $(CR^{5'}R^{5''})_t-C_{3-10}$ carbocyclic residue substituted with 0-5 R^{16} and a $(CR^{5'}R^{5''})_t-5-10$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{16} ;

$R^{5'}$ and $R^{5''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^6 , at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CF_2)_rCF_3$, CN, $(CH_2)_rNR^{6a}R^{6a'}$, $(CH_2)_rOH$, $(CH_2)_rOR^{6b}$, $(CH_2)_rSH$, $(CH_2)_rSR^{6b}$, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{6b}$, $(CH_2)_rC(O)NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}C(O)R^{6a}$, $(CH_2)_rC(O)OR^{6b}$, $(CH_2)_rOC(O)R^{6b}$, $(CH_2)_rS(O)_pR^{6b}$, $(CH_2)_rS(O)_2NR^{6a}R^{6a'}$,

$(\text{CH}_2)_r\text{NR}^{6d}\text{S}(\text{O})_2\text{R}^{6b}$, and $(\text{CH}_2)_t\text{phenyl}$ substituted
with 0-3 R^{6c} ;

5 R^{6a} and $\text{R}^{6a'}$, at each occurrence, are selected from H,
 C_{1-6}
alkyl, C_{3-6} cycloalkyl, and phenyl substituted with
0-3 R^{6c} ;

10 R^{6b} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{3-6}
cycloalkyl, and phenyl substituted with 0-3 R^{6c} ;

R^{6c} , at each occurrence, is selected from C_{1-6} alkyl, C_{3-6}
cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(\text{CF}_2)_r\text{CF}_3$,
15 $(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{SC}_{1-5}$ alkyl, and
 $(\text{CH}_2)_r\text{NR}^{6d}\text{R}^{6d}$;

R^{6d} , at each occurrence, is selected from H, C_{1-6} alkyl,
and C_{3-6} cycloalkyl;

20
with the proviso that when any of J, K, or L is CR^6R^6
and R^6 is halogen, cyano, nitro, or bonded to the
carbon to which it is attached through a
heteroatom, the other R^6 is not halogen, cyano, or
25 bonded to the carbon to which it is attached
through a heteroatom;

R^9 , is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8}
alkynyl, F, Cl, Br, I, NO_2 , CN, $(\text{CHR}')_r\text{OH}$,
30 $(\text{CH}_2)_r\text{OR}^{9d}$, $(\text{CH}_2)_r\text{SR}^{9d}$, $(\text{CH}_2)_r\text{NR}^{9a}\text{R}^{9a'}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OH}$,
 $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{9b}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^{9a}\text{R}^{9a'}$, $(\text{CH}_2)_r\text{NR}^{9a}\text{C}(\text{O})\text{R}^{9a}$,
 $(\text{CH}_2)_r\text{NR}^{9a}\text{C}(\text{O})\text{H}$, $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{9b}$, $(\text{CH}_2)_r\text{OC}(\text{O})\text{R}^{9b}$,
 $(\text{CH}_2)_r\text{OC}(\text{O})\text{NR}^{9a}\text{R}^{9a'}$, $(\text{CH}_2)_r\text{NR}^{9a}\text{C}(\text{O})\text{OR}^{9b}$,

(CH₂)_rS(O)_pR^{9b}, (CH₂)_rS(O)₂NR^{9a}R^{9a'},
 (CH₂)_rNR^{9a}S(O)₂R^{9b}, C₁₋₆ haloalkyl, a (CH₂)_r-C₃₋₁₀
 carbocyclic residue substituted with 0-5 R^{9c}, and a
 (CH₂)_r-5-10 membered heterocyclic system containing
 5 1-4 heteroatoms selected from N, O, and S,
 substituted with 0-3 R^{9c};

R^{9a} and R^{9a'}, at each occurrence, are selected from H,
 C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋
 10 10 carbocyclic residue substituted with 0-5 R^{9e},
 and a (CH₂)_r-5-10 membered heterocyclic system
 containing 1-4 heteroatoms selected from N, O, and
 S, substituted with 0-3 R^{9e};

15 alternatively, R^{9a} and R^{9a'}, along with the N to which
 they are attached, join to form a 5-6 membered
 heterocyclic system containing 1-2 heteroatoms
 selected from NR^{9g}, O, and S and optionally fused
 with a benzene ring or a 6-membered aromatic
 20 heterocycle;

R^{9b}, at each occurrence, is selected from C₁₋₆ alkyl,
 C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic
 residue substituted with 0-2 R^{9e}, and a (CH₂)_r-5-6
 25 membered heterocyclic system containing 1-4
 heteroatoms selected from N, O, and S, substituted
 with 0-3 R^{9e};

R^{9c}, at each occurrence, is selected from C₁₋₆ alkyl,
 30 C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_r-C₃₋₆ cycloalkyl,
 Cl, Br, I, F, (CF₂)_rCF₃, NO₂, CN, (CH₂)_rNR^{9f}R^{9f},
 (CH₂)_rOH, (CH₂)_rOR^{9b}, (CH₂)_rSR^{9b}, (CH₂)_rC(O)OH,
 (CH₂)_rC(O)R^{9b}, (CH₂)_rC(O)NR^{9f}R^{9f}, (CH₂)_rNR^{9f}C(O)R^{9a},

(CH₂)_rC(O)OR^{9b}, (CH₂)_rOC(O)R^{9b},
(CH₂)_rC(=NR^{9f})NR^{9f}R^{9f}, (CH₂)_rS(O)_pR^{9b},
(CH₂)_rNHC(=NR^{9f})NR^{9f}R^{9f}, (CH₂)_rS(O)₂NR^{9f}R^{9f},
(CH₂)_rNR^{9f}S(O)₂R^{9b}, and (CH₂)_rphenyl substituted
5 with 0-3 R^{9e};

R^{9d}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆
6 alkenyl, C₃₋₆ alkynyl, a C₃₋₁₀ carbocyclic residue
substituted with 0-3 R^{9c}, and a 5-6 membered
10 heterocyclic system containing 1-4 heteroatoms
selected from the group consisting of N, O, and S
substituted with 0-3 R^{9c};

R^{9e}, at each occurrence, is selected from C₁₋₆ alkyl,
15 C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl,
Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl,
OH, SH, (CH₂)_rSC₁₋₅ alkyl, (CH₂)_rNR^{9f}R^{9f}, and
(CH₂)_rphenyl, wherein the phenyl on the
(CH₂)_rphenyl is substituted with 0-5 substituents
20 selected from F, Cl, Br, I, NO₂, C₁₋₆alkyl, OH, and
NR^{9f}R^{9f};

R^{9f}, at each occurrence, is selected from H, C₁₋₆ alkyl,
and C₃₋₆ cycloalkyl;

25 R^{9g} is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl,
(CH₂)_rphenyl, C(O)R^{9f}, C(O)OR^{9h}, and SO₂R^{9h};

R^{9h}, at each occurrence, is selected from C₁₋₆ alkyl, and
30 C₃₋₆ cycloalkyl;

R^{10} , is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, F, Cl, Br, I, NO_2 , CN, $(CHR')_rOH$,
 $(CH_2)_rOR^{10d}$, $(CH_2)_rSR^{10d}$, $(CH_2)_rNR^{10a}R^{10a'}$,
 $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{10b}$, $(CH_2)_rC(O)NR^{10a}R^{10a'}$,
5 $(CH_2)_rNR^{10a}C(O)R^{10a}$, $(CH_2)_rNR^{10a}C(O)H$,
 $(CH_2)_rC(O)OR^{10b}$, $(CH_2)_rOC(O)R^{10b}$,
 $(CH_2)_rOC(O)NR^{10a}R^{10a'}$, $(CH_2)_rNR^{10a}C(O)OR^{10b}$,
 $(CH_2)_rS(O)_pR^{10b}$, $(CH_2)_rS(O)_2NR^{10a}R^{10a'}$,
 $(CH_2)_rNR^{10a}S(O)_2R^{10b}$, C_{1-6} haloalkyl, a $(CH_2)_r-C_{3-10}$
10 carbocyclic residue substituted with 0-5 R^{10c} , and
a $(CH_2)_r-5-10$ membered heterocyclic system
containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-3 R^{10c} ;

15 R^{10a} and $R^{10a'}$, at each occurrence, are selected from H,
 C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r-C_{3-10}$
10 carbocyclic residue substituted with 0-5 R^{10e} ,
and a $(CH_2)_r-5-10$ membered heterocyclic system
containing 1-4 heteroatoms selected from N, O, and
20 S, substituted with 0-3 R^{10e} ;

alternatively, R^{10a} and $R^{10a'}$, along with the N to which
they are attached, jointo form a 5-6 membered
heterocyclic system containing 1-2 heteroatoms
25 selected from NR^{10g} , O, and S and optionally fused
with a benzene ring or a 6-membered aromatic
heterocycle;

R^{10b} , at each occurrence, is selected from C_{1-6} alkyl,
30 C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r-C_{3-6}$ carbocyclic
residue substituted with 0-2 R^{10e} , and a $(CH_2)_r-5-6$
membered heterocyclic system containing 1-4

heteroatoms selected from N, O, and S, substituted with 0-3 R^{10e};

5 R^{10c}, at each occurrence, is selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, Br, I, F, (CF₂)_rCF₃, NO₂, CN, (CH₂)_rNR^{10f}R^{10f}, (CH₂)_rOH, (CH₂)_rOR^{10b}, (CH₂)_rSR^{10b}, (CH₂)_rC(O)OH, (CH₂)_rC(O)R^{10b}, (CH₂)_rC(O)NR^{10f}R^{10f}, (CH₂)_rNR^{10f}C(O)R^{10a}, (CH₂)_rC(O)OR^{10b}, (CH₂)_rOC(O)R^{10b}, 10 (CH₂)_rC(=NR^{10f})NR^{10f}R^{10f}, (CH₂)_rS(O)_pR^{10b}, (CH₂)_rNHC(=NR^{10f})NR^{10f}R^{10f}, (CH₂)_rS(O)₂NR^{10f}R^{10f}, (CH₂)_rNR^{10f}S(O)₂R^{10b}, and (CH₂)_rphenyl substituted with 0-3 R^{10e};

15 R^{10d}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆ alkenyl, C₃₋₆ alkynyl, and a C₃₋₁₀ carbocyclic residue substituted with 0-3 R^{10c};

20 R^{10e}, at each occurrence, is selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl, OH, SH, (CH₂)_rSC₁₋₅ alkyl, (CH₂)_rNR^{10f}R^{10f}, and (CH₂)_rphenyl;

25 R^{10f}, at each occurrence, is selected from H, C₁₋₆ alkyl, and C₃₋₆ cycloalkyl;

R^{10g} is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, (CH₂)_rphenyl, C(O)R^{10f}, SO₂R^{10h}, and C(O)O R^{10h};

30 R^{10h}, at each occurrence, is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl;

alternatively, R⁹ and R¹⁰ join to form =O, a C₃₋₁₀ cycloalkyl, a 5-6-membered lactone or lactam, or a 4-6-membered saturated heterocycle containing 1-2 heteroatoms selected from O, S, and NR^{10g} and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

with the proviso that when either of R⁹ or R¹⁰ is bonded to the carbon to which it is attached through a heteroatom, then the other of R⁹ or R¹⁰ is not halogen, cyano, or bonded to the carbon to which it is attached through a heteroatom;

R¹¹, is selected from H, C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CR'R¹⁷)_qOH, (CH₂)_qSH, (CR'R¹⁷)_qOR^{11d}, (CH₂)_qSR^{11d}, (CR'R¹⁷)_qNR^{11a}R^{11a'}, (CH₂)_rC(O)OH, (CH₂)_rC(O)R^{11b}, (CH₂)_rC(O)NR^{11a}R^{11a'}, (CH₂)_qNR^{11a}C(O)R^{11a}, (CH₂)_qOC(O)NR^{11a}R^{11a'}, (CH₂)_qNR^{11a}C(O)OR^{11b}, (CH₂)_qNR^{11a}C(O)NHR^{11a}, (CH₂)_rC(O)OR^{11b}, (CH₂)_qOC(O)R^{11b}, (CH₂)_qS(O)_pR^{11b}, (CH₂)_qS(O)₂NR^{11a}R^{11a'}, (CH₂)_qNR^{11a}S(O)₂R^{11b}, C₁₋₆ haloalkyl, a (CH₂)_r-C₃₋₁₀ carbocyclic residue substituted with 0-5 R^{11c}, and a (R'R¹⁷)_r-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{11c};

R^{11a} and R^{11a'}, at each occurrence, are selected from H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₁₀ carbocyclic residue substituted with 0-5 R^{11e}, and a (CH₂)_r-5-10 membered heterocyclic system

containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{11e};

alternatively, R^{11a} and R^{11a'} along with the N to which they are attached, jointly form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{11g}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{11b}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-2 R^{11e}, and a (CH₂)_r-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{11e};

R^{11c}, at each occurrence, is selected from C₁₋₆ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, Br, I, F, (CF₂)_rCF₃, NO₂, CN, (CH₂)_rNR^{11f}R^{11f}, (CH₂)_rOH, (CH₂)_rOC₁₋₄ alkyl, (CH₂)_rSC₁₋₄ alkyl, (CH₂)_rC(O)OH, (CH₂)_rC(O)R^{11b}, (CH₂)_rC(O)NR^{11f}R^{11f}, (CH₂)_rNR^{11f}C(O)R^{11a}, (CH₂)_rC(O)OC₁₋₄ alkyl, (CH₂)_rOC(O)R^{11b}, (CH₂)_rC(=NR^{11f})NR^{11f}R^{11f}, (CH₂)_rNHC(=NR^{11f})NR^{11f}R^{11f}, (CH₂)_rS(O)_pR^{11b}, (CH₂)_rS(O)₂NR^{11f}R^{11f}, (CH₂)_rNR^{11f}S(O)₂R^{11b}, and (CH₂)_rphenyl substituted with 0-3 R^{11e};

R^{11d}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆ alkenyl, C₃₋₆ alkynyl, and a C₃₋₁₀ carbocyclic residue substituted with 0-3 R^{11c};

R^{11e} , at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{11f}R^{11f}$, and
 5 $(CH_2)_rphenyl$, wherein the phenyl on the $(CH_2)_rphenyl$ is substituted with 0-5 substituents selected from F, Cl, Br, I, NO_2 , $C_{1-6}alkyl$, OH, and $NR^{9f}R^{9f}$;

10 R^{11f} , at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{11g} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_rphenyl$, $C(O)R^{11f}$, $C(O)OR^{11h}$, and SO_2R^{11h} ;

15 R^{11h} , at each occurrence, is selected from C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{12} , is selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CHR')_qOH$, $(CH_2)_qSH$, $(CHR')_qOR^{12d}$,
 20 $(CH_2)_qSR^{12d}$, $(CHR')_qNR^{12a}R^{12a'}$, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{12b}$, $(CH_2)_rC(O)NR^{12a}R^{12a'}$, $(CH_2)_qNR^{12a}C(O)R^{12a}$, $(CH_2)_rOC(O)NR^{12a}R^{12a'}$, $(CH_2)_rNR^{12a}C(O)OR^{12b}$, $(CH_2)_qNR^{12a}C(O)NHR^{12a}$,
 25 $(CH_2)_rC(O)OR^{12b}$, $(CH_2)_qOC(O)R^{12b}$, $(CH_2)_qS(O)_pR^{12b}$, $(CH_2)_qS(O)_2NR^{12a}R^{12a'}$, $(CH_2)_qNR^{12a}S(O)_2R^{12b}$, C_{1-6} haloalkyl, a $(CH_2)_r-C_{3-10}$ carbocyclic residue substituted with 0-5 R^{12c} , and a $(R'R^{17})_{r-5-10}$ membered heterocyclic system containing 1-4
 30 heteroatoms selected from N, O, and S, substituted with 0-3 R^{12c} ;

R^{12a} and $R^{12a'}$, at each occurrence, are selected from H,
 C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$ - C_{3-10}
carbocyclic residue substituted with 0-5 R^{12e} ,
and a $(CH_2)_r$ -5-10 membered heterocyclic system
5 containing 1-4 heteroatoms selected from N, O, and
S, substituted with 0-3 R^{12e} ;

alternatively, R^{12a} and $R^{12a'}$, along with the N to which
they are attached, jointo form a 5-6 membered
10 heterocyclic system containing 1-2 heteroatoms
selected from NR^{12g} , O, and S and optionally fused
with a benzene ring or a 6-membered aromatic
heterocycle;

15 R^{12b} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$ - C_{3-6} carbocyclic
residue substituted with 0-2 R^{12e} , and a $(CH_2)_r$ -5-6
membered heterocyclic system containing 1-4
heteroatoms selected from N, O, and S, substituted
20 with 0-3 R^{12e} ;

 R^{12c} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r$ - C_{3-6} cycloalkyl,
Cl, Br, I, F, $(CF_2)_rCF_3$, NO_2 , CN, $(CH_2)_rNR^{12f}R^{12f}$,
25 $(CH_2)_rOH$, $(CH_2)_rOC_{1-4}$ alkyl, $(CH_2)_rSC_{1-4}$ alkyl,
 $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{12b}$, $(CH_2)_rC(O)NR^{12f}R^{12f}$,
 $(CH_2)_rNR^{12f}C(O)R^{12a}$, $(CH_2)_rC(O)OC_{1-4}$ alkyl,
 $(CH_2)_rOC(O)R^{12b}$, $(CH_2)_rC(=NR^{12f})NR^{12f}R^{12f}$,
 $(CH_2)_rNHC(=NR^{12f})NR^{12f}R^{12f}$, $(CH_2)_rS(O)_pR^{12b}$,
30 $(CH_2)_rS(O)_2NR^{12f}R^{12f}$, $(CH_2)_rNR^{12f}S(O)_2R^{12b}$, and
 $(CH_2)_r$ phenyl substituted with 0-3 R^{12e} ;

R^{12d} , at each occurrence, is selected from methyl, CF_3 , C_{2-6} alkyl substituted with 0-3 R^{12e} , C_{3-6} alkenyl, C_{3-6} alkynyl, and a C_{3-10} carbocyclic residue substituted with 0-3 R^{12c} ;

5

R^{12e} , at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{12f}R^{12f}$, and $(CH_2)_rphenyl$;

10

R^{12f} , at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

15 R^{12g} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_rphenyl$, $C(O)R^{12f}$, $C(O)OR^{12h}$, and SO_2R^{12h} ;

R^{12h} , at each occurrence, is selected from C_{1-6} alkyl, and C_{3-6} cycloalkyl;

20

alternatively, R^{11} and R^{12} join to form a C_{3-10} cycloalkyl, a 5-6-membered lactone or lactam, or a 4-6-membered saturated heterocycle containing 1-2 heteroatoms selected from O, S, and NR^{11g} and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

25

R^{13} , at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, $(CF_2)_wCF_3$, $(CH_2)_qNR^{13a}R^{13a'}$, $(CHR')_qOH$, $(CH_2)_qOR^{13b}$, $(CH_2)_qSH$, $(CH_2)_qSR^{13b}$, $(CH_2)_wC(O)OH$, $(CH_2)_wC(O)R^{13b}$, $(CH_2)_wC(O)NR^{13a}R^{13a'}$, $(CH_2)_qNR^{13d}C(O)R^{13a}$,

30

$(\text{CH}_2)_w\text{C}(\text{O})\text{OR}^{13b}$, $(\text{CH}_2)_q\text{OC}(\text{O})\text{R}^{13b}$, $(\text{CH}_2)_w\text{S}(\text{O})_p\text{R}^{13b}$,
 $(\text{CH}_2)_w\text{S}(\text{O})_2\text{NR}^{13a}\text{R}^{13a'}$, $(\text{CH}_2)_q\text{NR}^{13d}\text{S}(\text{O})_2\text{R}^{13b}$, and
 $(\text{CH}_2)_w$ -phenyl substituted with 0-3 R^{13c} ;

5 R^{13a} and $\text{R}^{13a'}$, at each occurrence, are selected from H,
 C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted
with 0-3 R^{13c} ;

R^{13b} , at each occurrence, is selected from C_{1-6} alkyl,
10 C_{3-6}
cycloalkyl, and phenyl substituted with 0-3 R^{13c} ;

R^{13c} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(\text{CF}_2)_r\text{CF}_3$,
15 $(\text{CH}_2)_r\text{OC}_{1-5}$ alkyl, $(\text{CH}_2)_r\text{OH}$, $(\text{CH}_2)_r\text{SC}_{1-5}$ alkyl, and
 $(\text{CH}_2)_r\text{NR}^{13d}\text{R}^{13d}$;

R^{13d} , at each occurrence, is selected from H, C_{1-6} alkyl,
and C_{3-6} cycloalkyl;

20 R^{14} , at each occurrence, is selected from H, C_{1-6} alkyl,
 C_{2-8} alkenyl, C_{2-8} alkynyl, $(\text{CH}_2)_r\text{C}_{3-6}$ cycloalkyl,
Cl, Br, I, F, NO_2 , CN, $(\text{CHR}')_r\text{NR}^{14a}\text{R}^{14a'}$, $(\text{CHR}')_r\text{OH}$,
 $(\text{CHR}')_r\text{O}(\text{CHR}')_r\text{R}^{14d}$, $(\text{CHR}')_r\text{SH}$, $(\text{CHR}')_r\text{C}(\text{O})\text{H}$,
25 $(\text{CHR}')_r\text{S}(\text{CHR}')_r\text{R}^{14d}$, $(\text{CHR}')_r\text{C}(\text{O})\text{OH}$,
 $(\text{CHR}')_r\text{C}(\text{O})(\text{CHR}')_r\text{R}^{14b}$, $(\text{CHR}')_r\text{C}(\text{O})\text{NR}^{14a}\text{R}^{14a'}$,
 $(\text{CHR}')_r\text{NR}^{14f}\text{C}(\text{O})(\text{CHR}')_r\text{R}^{14b}$, $(\text{CHR}')_r\text{OC}(\text{O})\text{NR}^{14a}\text{R}^{14a'}$,
 $(\text{CHR}')_r\text{NR}^{14f}\text{C}(\text{O})\text{O}(\text{CHR}')_r\text{R}^{14b}$, $(\text{CHR}')_r\text{C}(\text{O})\text{O}(\text{CHR}')_r\text{R}^{14d}$,
 $(\text{CHR}')_r\text{OC}(\text{O})(\text{CHR}')_r\text{R}^{14b}$, $(\text{CHR}')_r\text{C}(=\text{NR}^{14f})\text{NR}^{14a}\text{R}^{14a'}$,
30 $(\text{CHR}')_r\text{NHC}(=\text{NR}^{14f})\text{NR}^{14f}\text{R}^{14f}$, $(\text{CHR}')_r\text{S}(\text{O})_p(\text{CHR}')_r\text{R}^{14b}$,
 $(\text{CHR}')_r\text{S}(\text{O})_2\text{NR}^{14a}\text{R}^{14a'}$, $(\text{CHR}')_r\text{NR}^{14f}\text{S}(\text{O})_2(\text{CHR}')_r\text{R}^{14b}$,

C₁₋₆ haloalkyl, C₂₋₈ alkenyl substituted with 0-3
 R', C₂₋₈ alkynyl substituted with 0-3 R',
 (CHR')_rphenyl substituted with 0-3 R^{14e}, and a
 (CH₂)_r-5-10 membered heterocyclic system containing
 5 1-4 heteroatoms selected from N, O, and S,
 substituted with 0-2 R^{15e}, or two R¹⁴ substituents
 on adjacent atoms on ring A form to join a 5-6
 membered heterocyclic system containing 1-3
 heteroatoms selected from N, O, and S substituted
 10 with 0-2 R^{15e};

R^{14a} and R^{14a'}, at each occurrence, are selected from H,
 C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋
 10 carbocyclic residue substituted with 0-5 R^{14e},
 15 and a (CH₂)_r-5-10 membered heterocyclic system
 containing 1-4 heteroatoms selected from N, O, and
 S, substituted with 0-2 R^{14e};

R^{14b}, at each occurrence, is selected from C₁₋₆ alkyl,
 20 C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic
 residue substituted with 0-3 R^{14e}, and (CH₂)_r-5-6
 membered heterocyclic system containing 1-4
 heteroatoms selected from N, O, and S, substituted
 with 0-2 R^{14e};

25 R^{14d}, at each occurrence, is selected from C₃₋₈ alkenyl,
 C₃₋₈ alkynyl, methyl, CF₃, C₂₋₆ alkyl substituted
 with 0-3 R^{14e}, a (CH₂)_r-C₃₋₁₀ carbocyclic residue
 substituted with 0-3 R^{14e}, and a (CH₂)_r-5-6 membered
 30 heterocyclic system containing 1-4 heteroatoms
 selected from N, O, and S, substituted with 0-3
 R^{14e};

- R^{14e} , at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r C_{3-6}$ cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_r CF_3$, $(CH_2)_r OC_{1-5}$ alkyl, OH, SH, $(CH_2)_r SC_{1-5}$ alkyl, $(CH_2)_r NR^{14f} R^{14f}$, and
- 5 $(CH_2)_r$ phenyl;
- R^{14f} , at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;
- 10 R^{15} , at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_r C_{3-6}$ cycloalkyl, Cl, Br, I, F, NO_2 , CN, $(CR'R^{17})_r NR^{15a} R^{15a'}$, $(CR'R^{17})_r OH$, $(CR'R^{17})_r O(CHR')_r R^{15d}$, $(CR'R^{17})_r SH$, $(CR'R^{17})_r C(O)H$, $(CR'R^{17})_r S(CHR')_r R^{15d}$, $(CR'R^{17})_r C(O)OH$,
- 15 $(CR'R^{17})_r C(O)(CHR')_r R^{15b}$, $(CR'R^{17})_r C(O)NR^{15a} R^{15a'}$, $(CR'R^{17})_r NR^{15f} C(O)(CHR')_r R^{15b}$, $(CR'R^{17})_r OC(O)NR^{15a} R^{15a'}$, $(CR'R^{17})_r NR^{15f} C(O)O(CHR')_r R^{15b}$, $(CR'R^{17})_r NR^{15f} C(O)NR^{15f} R^{15f}$,
- 20 $(CR'R^{17})_r C(O)O(CHR')_r R^{15d}$, $(CR'R^{17})_r OC(O)(CHR')_r R^{15b}$, $(CR'R^{17})_r C(=NR^{15f})NR^{15a} R^{15a'}$, $(CR'R^{17})_r NHC(=NR^{15f})NR^{15f} R^{15f}$, $(CR'R^{17})_r S(O)_p(CHR')_r R^{15b}$, $(CR'R^{17})_r S(O)_2 NR^{15a} R^{15a'}$, $(CR'R^{17})_r NR^{15f} S(O)_2(CHR')_r R^{15b}$, C_{1-6} haloalkyl, C_{2-8}
- 25 alkenyl substituted with 0-3 R' , C_{2-8} alkynyl substituted with 0-3 R' , $(CR'R^{17})_r$ phenyl substituted with 0-3 R^{15e} , and a $(CH_2)_{r-5-10}$ membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted
- 30 with 0-2 R^{15e} ;

- R^{15a} and R^{15a'}, at each occurrence, are selected from H, C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₁₀ carbocyclic residue substituted with 0-5 R^{15e}, and a (CH₂)_r-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};
- alternatively, R^{15a} and R^{15a'}, along with the N to which they are attached, jointly form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;
- R^{15b}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, a (CH₂)_r-C₃₋₆ carbocyclic residue substituted with 0-3 R^{15e}, and (CH₂)_r-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};
- R^{15d}, at each occurrence, is selected from C₃₋₈ alkenyl, C₃₋₈ alkynyl, methyl, CF₃, C₂₋₆ alkyl substituted with 0-3 R^{15e}, a (CH₂)_r-C₃₋₁₀ carbocyclic residue substituted with 0-3 R^{15e}, and a (CH₂)_r-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15e};
- R^{15e}, at each occurrence, is selected from C₁₋₆ alkyl, 2-cyanoethyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_r-C₃₋₆ cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, (CH₂)_rOC₁₋₅ alkyl, OH, SH, (CH₂)_rSC₁₋₅ alkyl,

- (CH₂)_rNR^{15f}R^{15f}, (CH₂)_rphenyl, and a heterocycle substituted with 0-1 R^{15g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;
- 5 R^{15f}, at each occurrence, is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl;
- 10 R^{15g} is selected from methyl, ethyl, acetyl, and CF₃;
- R^{15h} is selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, (CH₂)_rphenyl, C(O)R^{15f}, C(O)OR¹⁵ⁱ, and SO₂R¹⁵ⁱ;
- 15 R¹⁵ⁱ, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl;
- R¹⁶, at each occurrence, is selected from C₁₋₈ alkyl, C₂₋₈ alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl, Cl, Br, I, F, NO₂, CN, (CHR')_rNR^{16a}R^{16a'}, (CHR')_rOH, (CHR')_rO(CHR')_rR^{16d}, (CHR')_rSH, (CHR')_rC(O)H, (CHR')_rS(CHR')_rR^{16d}, (CHR')_rC(O)OH, (CHR')_rC(O)(CHR')_rR^{16b}, (CHR')_rC(O)NR^{16a}R^{16a'}, (CHR')_rNR^{16f}C(O)(CHR')_rR^{16b}, (CHR')_rC(O)O(CHR')_rR^{16d}, (CHR')_rOC(O)(CHR')_rR^{16b}, (CHR')_rC(=NR^{16f})NR^{16a}R^{16a'}, (CHR')_rNHC(=NR^{16f})NR^{16f}R^{16f}, (CHR')_rS(O)_p(CHR')_rR^{16b}, (CHR')_rS(O)₂NR^{16a}R^{16a'}, (CHR')_rNR^{16f}S(O)₂(CHR')_rR^{16b}, C₁₋₆ haloalkyl, C₂₋₈ alkenyl substituted with 0-3 R', C₂₋₈ alkynyl substituted with 0-3 R', and (CHR')_rphenyl substituted with 0-3 R^{16e};
- 20
- 25
- 30

- R^{16a} and $R^{16a'}$, at each occurrence, are selected from H,
 C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$ - C_{3-10}
 carbocyclic residue substituted with 0-5 R^{16e} ,
 and a $(CH_2)_r$ -5-10 membered heterocyclic system
 5 containing 1-4 heteroatoms selected from N, O, and
 S, substituted with 0-2 R^{16e} ;
- R^{16b} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$ - C_{3-6} carbocyclic
 10 residue substituted with 0-3 R^{16e} , and a $(CH_2)_r$ -5-6
 membered heterocyclic system containing 1-4
 heteroatoms selected from N, O, and S, substituted
 with 0-2 R^{16e} ;
- 15 R^{16d} , at each occurrence, is selected from C_{3-8} alkenyl,
 C_{3-8} alkynyl, methyl, CF_3 , C_{2-6} alkyl substituted
 with 0-3 R^{16e} , a $(CH_2)_r$ - C_{3-10} carbocyclic residue
 substituted with 0-3 R^{16e} , and a $(CH_2)_r$ -5-6 membered
 heterocyclic system containing 1-4 heteroatoms
 20 selected from N, O, and S, substituted with 0-3
 R^{16e} ;
- R^{16e} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_r$ - C_{3-6} cycloalkyl,
 25 Cl, F, Br, I, CN, NO_2 , $(CF_2)_r$ - CF_3 , $(CH_2)_r$ - OC_{1-5} alkyl,
 OH, SH, $(CH_2)_r$ - SC_{1-5} alkyl, $(CH_2)_r$ - $NR^{16f}R^{16f}$, and
 $(CH_2)_r$ -phenyl;
- R^{16f} , at each occurrence, is selected from H, C_{1-5} alkyl,
 30 and C_{3-6} cycloalkyl, and phenyl;
- R^{17} , at each occurrence, is independently selected from
 H and methyl;

R', at each occurrence, is selected from H, C₁₋₆ alkyl,
 C₃₋₈ alkenyl, C₃₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl,
 and (CH₂)_rphenyl substituted with R^{15e};
 5
 g is selected from 0, 1, 2, 3, and 4;
 v is selected from 0, 1, and 2;
 10 t is selected from 1 and 2;
 w is selected from 0 and 1;
 r is selected from 0, 1, 2, 3, 4, and 5;
 15 q is selected from 1, 2, 3, 4, and 5; and
 p is selected from 0, 1, and 2.
 20 2. The compound of claim 1, wherein:
 Z is selected from O, S, N(CN), and N(CONH₂);
 R² is selected from H and C₁₋₄ alkyl;
 25 R⁶, at each occurrence, is selected from C₁₋₄ alkyl, C₂₋₈
 alkenyl, C₂₋₈ alkynyl, (CH₂)_rC₃₋₆ cycloalkyl,
 (CF₂)_rCF₃, CN, (CH₂)_rOH, (CH₂)_rOR^{6b}, (CH₂)_rC(O)R^{6b},
 (CH₂)_rC(O)NR^{6a}R^{6a'}, (CH₂)_rNR^{6d}C(O)R^{6a}, and
 30 (CH₂)_tphenyl substituted with 0-3 R^{6c};
 R^{6a} and R^{6a'}, at each occurrence, are selected from H,
 C₁₋₆

alkyl, C₃₋₆ cycloalkyl, and phenyl substituted with
0-3 R^{6c};

R^{6b}, at each occurrence, is selected from C₁₋₆ alkyl,
5 C₃₋₆
cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6c}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆
6 cycloalkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃,
10 (CH₂)_rOC₁₋₅ alkyl, (CH₂)_rOH, (CH₂)_rSC₁₋₅ alkyl, and
(CH₂)_rNR^{6d}R^{6d};

R^{6d}, at each occurrence, is selected from H, C₁₋₆ alkyl,
and C₃₋₆ cycloalkyl;

15 R¹³, at each occurrence, is selected from C₁₋₄ alkyl, C₃₋₆
6 cycloalkyl, (CH₂)NR^{13a}R^{13a'}, (CHR')OH, (CH₂)OR^{13b},
(CH₂)_wC(O)R^{13b}, (CH₂)_wC(O)NR^{13a}R^{13a'},
(CH₂)NR^{13d}C(O)R^{13a}, (CH₂)_wS(O)₂NR^{13a}R^{13a'},
20 (CH₂)NR^{13d}S(O)₂R^{13b}, and (CH₂)_w-phenyl substituted
with 0-3 R^{13c};

R^{13a} and R^{13a'}, at each occurrence, are selected from H,
C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and phenyl substituted
25 with 0-3 R^{13c};

R^{13b}, at each occurrence, is selected from C₁₋₆ alkyl,
C₃₋₆
cycloalkyl, and phenyl substituted with 0-3 R^{13c};
30

R^{13c} , at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2 , $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, and $(CH_2)_rNR^{13d}R^{13d}$;

5 R^{13d} , at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

v is selected from 0, 1 and 2;

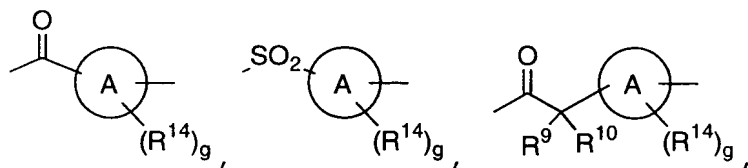
10 q is selected from 1, 2, and 3; and

r is selected from 0, 1, 2, and 3.

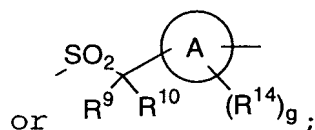
3. The compound of claim 2, wherein:

15

E is $-(C=O)-(CR^9R^{10})_v-(CR^{11}R^{12})-$, $-(SO_2)-(CR^9R^{10})_v-(CR^{11}R^{12})-$,



20



25

R^3 is selected from $(CH_2)_2N(CH_3)_2$, a $(CR^{3'}H)_r$ -carbocyclic residue substituted with 0-5 R^{15} , wherein the carbocyclic residue is selected from phenyl, C_{3-6} cycloalkyl, naphthyl, and adamantyl; and a $(CR^{3'}H)_r$ -heterocyclic system substituted with 0-3 R^{15} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl,

R^{16a} and R^{16a'}, at each occurrence, are selected from H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and (CH₂)_rphenyl substituted with 0-3 R^{16e};

5

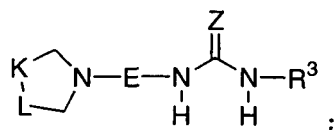
R^{16b}, at each occurrence, is selected from C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and (CH₂)_rphenyl substituted with 0-3 R^{16e};

10 R^{16d}, at each occurrence, is selected from C₁₋₆ alkyl and phenyl;

R^{16e}, at each occurrence, is selected from C₁₋₆ alkyl, Cl, F, Br, I, CN, NO₂, (CF₂)_rCF₃, OH, and (CH₂)_rOC₁₋₅ alkyl; and

R^{16f}, at each occurrence, is selected from H, and C₁₋₅ alkyl.

20 5. The compound of claim 3, wherein the compound formula (I) is:



25

R¹⁶, at each occurrence, is selected from C₁₋₈ alkyl, (CH₂)_rC₃₋₆ cycloalkyl, CF₃, Cl, Br, I, F, (CH₂)_rNR^{16a}R^{16a'}, NO₂, CN, OH, (CH₂)_rOR^{16d}, (CH₂)_rC(O)R^{16b}, (CH₂)_rC(O)NR^{16a}R^{16a'}, (CH₂)_rNR^{16f}C(O)R^{16b}, (CH₂)_rS(O)_pR^{16b},

30

$(\text{CH}_2)_r\text{S}(\text{O})_2\text{NR}^{16a}\text{R}^{16a'}$, $(\text{CH}_2)_r\text{NR}^{16f}\text{S}(\text{O})_2\text{R}^{16b}$, and
 $(\text{CH}_2)_r\text{phenyl}$ substituted with 0-3 R^{16e} ;

R^{16a} and $\text{R}^{16a'}$, at each occurrence, are selected from H,
 5 C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(\text{CH}_2)_r\text{phenyl}$
 substituted with 0-3 R^{16e} ;

R^{16b} , at each occurrence, is selected from C_{1-6} alkyl,
 C_{3-6} cycloalkyl, and $(\text{CH}_2)_r\text{phenyl}$ substituted with
 10 0-3 R^{16e} ;

R^{16d} , at each occurrence, is selected from C_{1-6} alkyl and
 phenyl;

15 R^{16e} , at each occurrence, is selected from C_{1-6} alkyl,
 Cl , F , Br , I , CN , NO_2 , $(\text{CF}_2)_r\text{CF}_3$, OH , and $(\text{CH}_2)_r\text{OC}_{1-5}$
 alkyl; and

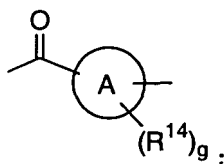
R^{16f} , at each occurrence, is selected from H, and C_{1-5}
 20 alkyl.

6. The compound of claim 4, wherein:

R^5 is CH_2phenyl substituted with 0-3 R^{16} ;

25

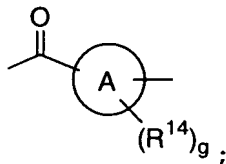
E is $-(\text{C}=\text{O})-(\text{CR}^9\text{R}^{10})_v-(\text{CR}^{11}\text{R}^{12})_-$, or



30 r is selected from 0, 1, and 2.

7. The compound of claim 5, wherein:

E is $-(C=O)-(CR^9R^{10})_v-(CR^{11}R^{12})-$, or



R^5 is CH_2 phenyl substituted with 0-3 R^{16} ; and

r is selected from 0, 1, and 2.

8. The compound of claim 6, wherein:

J is selected from CH_2 and CHR^5 ;

15 K is selected from CH_2 and CHR^5 ;

L is selected from CH_2 and CHR^5 ;

20 R^3 is a $(CH_2)_r-C_{3-10}$ carbocyclic residue substituted with 0-3 R^{15} , wherein the carbocyclic residue is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$ -heterocyclic system substituted with 0-3 R^{15} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, 25 piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-

triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

9. The compound of claim 7, wherein:

5

K is selected from CH_2 and CHR^5 ;

L is selected from CH_2 and CHR^5 ; and

10 R^3 is a $(\text{CH}_2)_r\text{-C}_{3-10}$ carbocyclic residue substituted with 0-3 R^{15} , wherein the carbocyclic residue is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(\text{CR}^{3'}\text{H})_r$ -heterocyclic system substituted with 0-3
15 R^{15} , wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl,
20 indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

25 10. The compound of claim 3, wherein:

M is absent or selected from CH_2 ;

Q is CH_2 ;

30

J is CH_2 ;

K and L are independently selected from CH_2 and CHR^5 ;

Z is O, S, NCN, or NCONH₂;

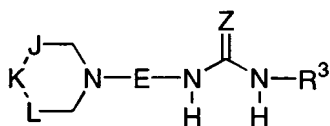
R¹ is H;

5 R² is H;

R³ is selected from a (CH₂)_rN(CH₃)₂, a (CH₂)_r-C₃₋₁₀
carbocyclic residue substituted with 0-3 R¹⁵,
wherein the carbocyclic residue is selected from
10 cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,
phenyl, naphthyl and adamantyl, and a (CR^{3'}H)_r-
heterocyclic system substituted with 0-3 R¹⁵,
wherein the heterocyclic system is selected from
pyridinyl, thiophenyl, furanyl, indazolyl,
15 benzothiazolyl, benzimidazolyl, benzothiophenyl,
benzofuranyl, benzoxazolyl, benzisoxazolyl,
quinolinyl, isoquinolinyl, imidazolyl, indolyl,
indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl,
piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-
20 triazolyl, tetrazolyl, thiadiazolyl, thiazolyl,
oxazolyl, pyrazinyl, and pyrimidinyl; and

R⁵ is selected from a CH₂-phenyl substituted with 0-5
R¹⁶ and a CH₂-heterocyclic system substituted with
25 0-3 R¹⁶, wherein the heterocyclic system is
selected from pyridinyl, thiophenyl, furanyl,
indazolyl, benzothiazolyl, benzimidazolyl,
benzothiophenyl, benzofuranyl, benzoxazolyl,
benzisoxazolyl, quinolinyl, isoquinolinyl,
30 imidazolyl, indolyl, indolinyl, isoindolyl,
isothiadiazolyl, isoxazolyl, piperidinyl,
pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl,
tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl,
pyrazinyl, and pyrimidinyl.

11. The compound of formula (II) of claim 8:

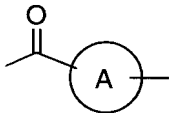


(II)

or stereoisomers or pharmaceutically acceptable salts thereof, wherein:

J, K, and L are independently selected from CH_2 and CHR^5 ;

Z is selected from O, and $\text{N}(\text{CN})$;

E is $-(\text{C}=\text{O})-(\text{CR}^9\text{R}^{10})_v-\text{CR}^{11}\text{R}^{12}-$, or ;

Ring A is cyclohexyl;

R^3 is selected from $(\text{CH}_2)_r\text{N}(\text{CH}_3)_2$, cyclopropyl, $-\text{CH}_2-$ cyclopropyl, phenyl substituted with 0-2 R^{15} ; and a $(\text{CH}_2)_r$ -5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15} , wherein the heterocyclic system is selected from morpholinyl, pyridinyl, and thiazolyl;

R^5 is selected from a $-\text{CH}_2$ -phenyl substituted with 0-2 R^{16} ;

R^9 is selected from H, OH, $\text{N}(\text{CO})\text{CH}_3$, and $\text{NR}^{9a}\text{R}^{9a'}$;

R^{9a} and $R^{9a'}$, at each occurrence, are selected from H,
 methyl, ethyl, propyl, butyl, i-butyl;

5 alternatively, R^9 and R^{10} join to form cyclohexyl;

R^{11} is selected from H, methyl, $(CH_2)_rCONR^{11a}R^{11a'}$,
 $C(O)OR^{11b}$, and a (CH_2) -heterocyclic system, wherein
 the heterocyclic system is selected from

10 morpholinyl and piperidinyl;

R^{11a} and $R^{11a'}$ are independently selected from H, methyl,
 ethyl, propyl, i-propyl, butyl, i-butyl and t-
 butyl;

15 alternatively, R^{11a} and $R^{11a'}$ along with the N to which
 they are attached, join to form a 5-6 membered
 heterocyclic system, wherein the heterocyclic
 system is selected from morpholinyl, piperidinyl,

20 pyrrolidinyl, azapanyl, and N-methylpiperazinyl;

R^{11b} is CH_2 -phenyl;

R^{11g} is selected from H, methyl, ethyl, propyl, i-
 25 propyl, $C(O)OR^{11h}$, and SO_2R^{11h} ;

R^{11h} is selected from methyl, ethyl, propyl, i-propyl,
 butyl, i-butyl and t-butyl;

30 R^{12} is H;

or alternatively, R^{11} and R^{12} join to form cyclopropyl,
 cyclopentyl, cyclohexyl, benzocyclopentyl,
 benzocyclohexyl, tetrahydropyan, tetrahydrofuran,

or a 5-6-membered saturated heterocycle containing
 NR^{11g} selected from pyrrolidine, and piperidine
 ring;

5 R¹⁵, at each occurrence, is selected from methyl, ethyl,
 propyl, i-propyl, butyl, i-butyl, pentyl, CF₃, Cl,
 Br, I, F, NO₂, CN, OH, OCH₃, C(O)OR^{15b}, C(O)OH,
 C(O)CH₃, C(O)NR^{15a}R^{15a'} and a 5-6 membered
 heterocyclic system containing 1-4 heteroatoms
 10 selected from N, O, and S, substituted with 0-2
 R^{15e}, wherein the heterocyclic system is selected
 from triazolyl, imidazolyl, tetrazolyl, pyrazolyl,
 oxazolyl, and isoxazolyl;

15 R^{15a} and R^{15a'} are selected from hydrogen, methyl, ethyl,
 propyl, i-propyl, butyl, t-butyl, and a
 heterocyclic system containing 1-4 heteroatoms
 selected from N, O, and S, substituted with 0-2
 R^{15e}, wherein the heterocyclic system is selected
 20 from morpholinyl;

R^{15b} is selected from methyl and benzyl;

25 R^{15e} is selected from methyl, ethyl and 2-cyanoethyl;

R¹⁶, at each occurrence, is selected from Cl, Br, I, and
 F,

30 v is 0 or 1; and

r is 0, 1, or 2.

12. The compound of claim 1 wherein the compound is
 selected from:

- N-(3,5-diacetylphenyl)-N'-[3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxopropyl]-urea;
- 5 N''-cyano-N-(3,5-diacetylphenyl)-N'-[3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxopropyl]-guanidine;
- 10 N-(3-acetylphenyl)-N'-[(1S,2S)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 15 N-(3-acetylphenyl)-N'-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 20 N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[4-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- 25 N''-cyano-N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[4-(1-methyl-1H-tetrazol-5-yl)phenyl]-guanidine;
- 30 N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-(4-pyridinyl)-urea;

- N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[2-(4-morpholinyl)ethyl]-urea;
- 5 N''-cyano-N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-guanidine;
- 10 N-[2-(dimethylamino)ethyl]-N'-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 15 N-(5-acetyl-4-methyl-2-thiazolyl)-N'-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 20 N-(3-acetylphenyl)-N'-[1-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 25 N-[3,5-bis(1-methyl-1H-tetrazol-5-yl)phenyl]-N'-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 30 N-[3,5-di(1H-imidazol-1-yl)phenyl]-N'-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- N-[3,5-di(1H-1,2,4-triazol-1-yl)phenyl]-N'-[(1R,2R)-2-[[(3S)-3-[(4-

fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl
]-urea;

5 N-(3-acetylphenyl)-N'-[1-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]cyclopentyl]-urea;

10 N-(3-acetylphenyl)-N'-[1-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]-urea;

15 N-(3-acetylphenyl)-N'-[2-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]-2,3-
dihydro-1H-inden-2-yl]-urea;

N-(3-acetylphenyl)-N'-[2-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]-1,2,3,4-
tetrahydro-2-naphthalenyl]-urea;

20 N-(5-acetyl-4-methyl-2-thiazolyl)-N'-[1-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]-urea;

25 N-(3-acetylphenyl)-N'-[2-[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]-2-oxoethyl]-urea;

30 N-[3,5-bis(1-ethyl-1H-tetrazol-5-yl)phenyl]-N'-[(1R,2R)-
2-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl
]-urea;

35 N-[1-[[(3S)-3-[(4-
fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;

- (alpha-1S,3S)-3-[(4-fluorophenyl)methyl]-alpha-[[[[3-(1-methyl-1H-tetrazol-5-yl)phenyl]amino]carbonyl]amino]-gamma-oxo-1-piperidinebutanoic acid, phenylmethyl ester;
- 5 (alpha-1S,3S)-3-[(4-fluorophenyl)methyl]-N-methyl-alpha-[[[[3-(1-methyl-1H-tetrazol-5-yl)phenyl]amino]carbonyl]amino]-gamma-oxo-1-piperidinebutanamide;
- 10 N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-1-(4-morpholinylcarbonyl)-3-oxopropyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- 15 3-[[[[(1R,2R)-2-[[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]amino]carbonyl]amino]-benzoic acid, ethyl ester;
- 20 3-[[[[(1R,2R)-2-[[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]amino]carbonyl]amino]benzoic acid;
- N-[1-[[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]-N'-[3-(4-morpholinylcarbonyl)phenyl]-urea;
- 25 N-[(1R,2R)-2-[[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[2-methoxy-5-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- 30 N-[3-[1-(2-cyanoethyl)-1H-tetrazol-5-yl]phenyl]-N'-[(1R,2R)-2-[[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-urea;
- 35

- N-[(1R,2R)-2-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclohexyl]-N'-[3-(1H-tetrazol-5-yl)phenyl]-urea;
- 5 3-[[[1-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]amino]carbonyl]amino]-4-methoxy-N-methylbenzamide;
- 10 N-[1-[[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]-N'-[2-methoxy-5-(4-morpholinylcarbonyl)phenyl]-urea;
- 15 N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxo-1-(1-pyrrolidinylcarbonyl)propyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- 20 -(alpha-1S,3S)-N-(1,1-dimethylethyl)-3-[(4-fluorophenyl)methyl]-alpha-[[[3-(1-methyl-1H-tetrazol-5-yl)phenyl]amino]carbonyl]amino]-gamma-oxo-1-piperidinebutanamide,
- 25 N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxo-1-(1-piperidinylcarbonyl)propyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;
- 30 N-(3-acetylphenyl)-N'-[(2S)-2-amino-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxopropyl]-urea;
- N-(3-acetylphenyl)-N'-[(2R)-2-amino-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-3-oxopropyl]-urea;

3-[[[1-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]carbonyl]cyclopropyl]amino]carbonyl]amino]-4-methoxybenzamide;

5 N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-1-[(4-methyl-1-piperazinyl)carbonyl]-3-oxopropyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;

10 N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-urea;

15 N''-cyano-N-[(1S)-3-[(3S)-3-[(4-fluorophenyl)methyl]piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]-N'-[3-(1-methyl-1H-tetrazol-5-yl)phenyl]-guanidine

20 3-[(4-fluorophenyl)methyl]-N,N-dimethyl- α -[[[3-(1-methyl-1H-tetrazol-5-yl)phenyl]amino]carbonyl]amino]- γ -oxo-(α -1S,3S)-1-piperidinebutanamide

25 N-{(1S)-1-({[(3-acetylanilino)carbonyl]amino)methyl)-2-[(3S)-3-(4-fluorobenzyl)piperidinyl]-2-oxoethyl}acetamide;

30 N-{(1R)-1-({[(3-acetylanilino)carbonyl]amino)methyl)-2-[(3S)-3-(4-fluorobenzyl)piperidinyl]-2-oxoethyl}acetamide;

35 3-[[[(1S)-3-[(3S)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]amino]carbonyl]amino]-N-methylbenzamide;

- N*-(3-chlorophenyl)-*N'*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]urea;
- 5 *N*-(3-cyanophenyl)-*N'*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]urea;
- 10 *N*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]-*N'*-(3-methoxyphenyl)urea;
- 15 *N*-cyclopropyl-*N'*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]urea
- 20 *N*-(cyclopropylmethyl)-*N'*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]urea;
- benzyl 3-[([{ (1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(4-morpholinylmethyl)-3-oxopropyl]amino } carbonyl] amino]-4-methoxybenzoate;
- 25 *N*-(5-acetyl-4-methyl-1,3-thiazol-2-yl)-*N'*-[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxo-1-(1-piperidinylmethyl)propyl]urea;
- 30 *N*-[(1*S*,2*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-methyl-1-(4-morpholinylcarbonyl)-3-oxopropyl]-*N'*-[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
- 35 3-[([{ (1*S*,2*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-methyl-1-(4-morpholinylcarbonyl)-3-oxopropyl]amino } carbonyl] amino]-*N*-methylbenzamide;

N -(3,5-diacetylphenyl)- N' -{(1*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-methyl-3-oxopropyl}urea;
5
 N -{(1*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-methyl-3-oxopropyl}- N' -[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
10
 N -{(2*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-methyl-3-oxopropyl}- N' -[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
15
 N -(3-acetylphenyl)- N' -{(1*S*)-1-[[*tert*-butyl(methyl)amino]methyl]-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxopropyl}urea;
20
 N -{(2*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-methyl-3-oxopropyl}- N' -[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
25
(2*S*)- N -cyclopropyl-4-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-[[{3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]amino}carbonyl)amino]-4-oxobutanamide;
30
 N -{(1*R*)-2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-[[{3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]amino}carbonyl)amino]methyl}-2-oxoethyl)acetamide;

 N -[(1*S*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-(hexahydro-1*H*-azepin-1-ylcarbonyl)-3-oxopropyl]- N' -[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;

- N*-(1-{2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-oxoethyl}cyclopropyl)-*N'*-[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
- 5 *N*-{(1*R*)-2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-[[[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]amino]carbonyl]amino)methyl}-2-oxoethyl)-2,2-dimethylpropanamide;
- 10 *N*-{(1*R*)-1-[[[(5-acetyl-4-methyl-1,3-thiazol-2-yl)amino]carbonyl]amino)methyl]-2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-oxoethyl}-2,2-dimethylpropanamide;
- 15 *N*-{(1*S*)-1-{[*tert*-butyl(methyl)amino]methyl}-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxopropyl}-*N'*-[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
- 20 *N*-(5-acetyl-4-methyl-1,3-thiazol-2-yl)-*N'*-{(2*R*)-2-(diisobutylamino)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxopropyl}urea;
- 25 *N*-{(2*R*)-2-(diisobutylamino)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxopropyl}-*N'*-[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
- 30 *N*-(5-acetyl-4-methyl-1,3-thiazol-2-yl)-*N'*-{(1*S*)-1-{[*tert*-butyl(methyl)amino]methyl}-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-3-oxopropyl}urea;
- 30 *N*-{(1*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-methyl-3-oxopropyl}-*N'*-(4-pyridinyl)urea;

- N*-(5-acetyl-4-methyl-1,3-thiazol-2-yl)-*N'*-{(1*R*,2*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-hydroxy-1-methyl-3-oxopropyl}urea;
- 5 *N*-(3,5-diacetylphenyl)-*N'*-{(1*R*,2*R*)-3-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-2-hydroxy-1-methyl-3-oxopropyl}urea;
- 10 *N*-{3-[(dimethylamino)methyl]phenyl}-*N'*-(1*R*,2*R*)-2-[[(3*R*)-3-(4-fluorobenzyl)-1-piperidinyl]carbonyl]cyclohexyl}urea;
- 15 3-({[(1-{[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]carbonyl}cyclopropyl)amino]carbonyl}amino)benzamide;
- 20 *N*-(1-{[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]carbonyl}cyclopropyl)-*N'*-[2-methoxy-5-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea;
- 25 *N*-(1-{[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]carbonyl}cyclopropyl)-*N'*-[3-(5-methyl-1*H*-tetraazol-1-yl)phenyl]urea;
- 30 *N*-{(1*R*)-2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-methyl-2-oxoethyl}-*N'*-[3-(1-methyl-1*H*-tetraazol-5-yl)phenyl]urea; and
- 30 *N*-(3,5-diacetylphenyl)-*N'*-{(1*S*)-2-[(3*S*)-3-(4-fluorobenzyl)-1-piperidinyl]-1-methyl-2-oxoethyl}urea.

13. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a

therapeutically effective amount of a compound according to Claim 1.

14. A method for modulation of chemokine receptor activity comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1.

15. A method for treating or preventing asthma, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 1.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

20

17. The method of claim 14 wherein modulation of chemokine receptor activity comprises contacting a CCR3 receptor with an effective inhibitory amount of the compound.

25

18. A method for treating or preventing inflammatory disorders comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claim 12, or a pharmaceutically acceptable salt thereof.

30

19. A method according to Claim 18, wherein the disorder is selected from asthma, allergic rhinitis,

atopic dermatitis, inflammatory bowel diseases,
idiopathic pulmonary fibrosis, bullous pemphigoid,
helminthic parasitic infections, allergic colitis,
eczema, conjunctivitis, transplantation, familial
5 eosinophilia, eosinophilic cellulitis, eosinophilic
pneumonias, eosinophilic fasciitis, eosinophilic
gastroenteritis, drug induced eosinophilia, HIV
infection, cystic fibrosis, Churg-Strauss syndrome,
lymphoma, Hodgkin's disease, and colonic carcinoma.

10

20. The method according to Claim 19, wherein the
disorder is selected from asthma, allergic rhinitis,
atopic dermatitis, and inflammatory bowel diseases.

15

21. The method according to Claim 20, wherein the
disorder is asthma.